PB88-120506

Health and Environmental Effects Profile for Bromacil

(U.S.) Environmental Protection Agency
Cincinnati, OH

Dec 83

U.S. Department of Commerce
National Technical Information Service
NTIS

PB88-120506

EPA/600/X-84/122
December 1983

HEALTH AND ENVIRONMENTAL EFFECTS PROFILE FOR BROMACIL

ENVIRONMENTAL CRITERIA AND ASSESSMENT OFFICE
OFFICE OF HEALTH AND ENVIRONMENTAL ASSESSMENT
OFFICE OF RESEARCH AND DEVELOPMENT
U.S. ENVIRONMENTAL PROTECTION AGENCY
CINCINNATI, OH 45268

REPRODUCED BY
U.S. DEPARTMENT OF COMMERCE
NATIONAL TECHNICAL
INFORMATION SERVICE
SPRINGFIELD, VA. 22161

TECHNICAL REPORT DATA
(Please read Instructions on the reverse before completing)

1. REPORT NO. EPA/600/X-84/122	2.
3. RECIPIENT'S ACCESSION NO. PB88 120506/AS	
4. TITLE AND SUBTITLE Health and Environmental Effects Profile for Bromacil	5. REPORT DATE December 1983
	6. PERFORMING ORGANIZATION CODE
7. AUTHOR(S)	8. PERFORMING ORGANIZATION REPORT NO.
9. PERFORMING ORGANIZATION NAME AND ADDRESS	10. PROGRAM ELEMENT NO.
	11. CONTRACT/GRANT NO.
12. SPONSORING AGENCY NAME AND ADDRESS Environmental Criteria and Assessment Office Office of Research and Development U.S. Environmental Protection Agency Cincinnati, OH 45268	13. TYPE OF REPORT AND PERIOD COVERED
	14. SPONSORING AGENCY CODE EPA/600/22
15. SUPPLEMENTARY NOTES	

16. ABSTRACT

The Health and Environmental Effects Profile for Bromacil was prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA). Both published literature and information obtained from Agency program office files were evaluated as they pertained to potential human health, aquatic life and environmental effects of hazardous waste constituents.

Quantitative estimates have been presented provided sufficient data are available. Bromacil has been evaluated as a carcinogen. The human carcinogen potency factor (q_1^*) for Bromacil is 6.4×10^{-2} (mg/kg bw/day)$^{-1}$ for oral exposure.

Quantitative estimates have been presented provided sufficient data are available. Bromacil has been determined to be a systemic toxicant. An Acceptable Daily Intake (ADI), defined as the amount of a chemical to which humans can be exposed on a daily basis over an extended period of time (usually a lifetime) without suffering a deleterious effect, for Bromacil is 1.3×10^{-1} mg/kg bw/day for oral exposure.

17. KEY WORDS AND DOCUMENT ANALYSIS

a. DESCRIPTORS	b. IDENTIFIERS/OPEN ENDED TERMS	c. COSATI Field/Group

18. DISTRIBUTION STATEMENT Public	19. SECURITY CLASS (This Report) Unclassified	21. NO. OF PAGES 43
	20. SECURITY CLASS (This page) Unclassified	22. PRICE

EPA Form 2220-1 (Rev. 4-77) PREVIOUS EDITION IS OBSOLETE

DISCLAIMER

This document has been reviewed in accordance with U.S. Environmental Protection Agency policy and approved for publication. Mention of trade names or commercial products does not constitute endorsement or recommendation for use.

PREFACE

Health and Environmental Effects Profiles (HEEPs) are prepared for the Office of Solid Waste by the Office of Health and Environmental Assessment. The HEEPs are intended to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA). Both published literature and information obtained from Agency program office files are evaluated as they pertain to potential human health, aquatic life and environmental effects of hazardous waste constituents.The literature searched and the dates of the searches are included in the section titled "Appendix: Literature Searched."

Quantitative estimates are presented provided sufficient data are available. For systemic toxicants, these include, Acceptable Daily Intakes (ADIs) for chronic exposures. An ADI is defined as the amount of a chemical to which humans can be exposed on a daily basis over an extended period of time (usually a lifetime) without suffering a deleterious effect. In the case of suspected carcinogens, ADIs are not estimated in this document series. Instead, a carcinogenic potency factor or q_1^* is provided. These potency estimates are derived for both oral and inhalation exposures where possible. In addition, unit risk estimates for air and drinking water are presented based on inhalation and oral data, respectively.

The first draft of this document was prepared by Syracuse Research Corporation under EPA Contract No. 68-03-3228. The document was subsequently revised after reviews by staff within the Office of Health and Environmental Assessment: Carcinogen Assessment Group, Reproductive Effects Assessment Group, Exposure Assessment Group, and the Environmental Criteria and Assessment Office in Cincinnati.

The HEEPs will become part of the EPA RCRA docket.

ACKNOWLEDGEMENTS

The initial draft of this report was prepared by Syracuse Research Corporation under Contract No. 68-03-3228 for U.S. EPA's Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH. Dr. Christopher DeRosa was the Technical Project Monitor and Helen Ball was the Project Officer. The final documents in this series were prepared for the Office of Solid Waste, Washington, D.C.

Scientists from the following U.S. EPA offices provided review comments for this document series:

Environmental Criteria and Assessment Office, Cincinnati, OH
Carcinogen Assessment Group
Exposure Assessment Group
Reproductive Effects Assessment Group

Editorial review for the document series was provided by:
Judith Olsen and Erma Durden
Environmental Criteria and Assessment Office, Cincinnati, OH

Technical support services for this document series were provided by:
Bette Zwayer, Pat Daunt, Karen Mann, and Jacky Bohanon
Environmental Criteria and Assessment Office, Cincinnati, OH.

TABLE OF CONTENTS

		Page
1.	INTRODUCTION	1
1.1.	STRUCTURE AND CAS NUMBER	1
1.2.	PHYSICAL AND CHEMICAL PROPERTIES	1
1.3.	PRODUCTION DATA	2
1.4.	USAGE DATA	2
2.	ENVIRONMENTAL FATE AND TRANSPORT	4
3.	EXPOSURE	9
4.	COMPOUND DISPOSITION AND PHARMACOKINETICS	10
4.1.	ABSORPTION	10
4.2.	DISTRIBUTION	10
4.3.	METABOLISM	10
4.4.	EXCRETION	11
5.	EFFECTS	12
5.1.	CARCINOGENICITY	12
5.2.	MUTAGENICITY	12
5.3.	TERATOGENICITY	17
5.4.	OTHER REPRODUCTIVE EFFECTS	18
5.5.	CHRONIC AND SUBCHRONIC TOXICITY	18
5.6.	OTHER RELEVANT INFORMATION	19
6.	AQUATIC TOXICITY	21
6.1.	ACUTE TOXICITY	21
6.2.	CHRONIC TOXICITY	21
6.3.	PLANT EFFECTS	21
6.4.	RESIDUES	21
6.5	OTHER RELEVANT INFORMATION	21
7.	EXISTING GUIDELINES AND STANDARDS	22
7.1.	HUMAN	22
7.2.	AQUATIC	22
8.	RISK ASSESSMENT	23
9.	REFERENCES	26
APPENDIX		34

LIST OF TABLES

No.	Title	Page
1-1	Average Annual Usage of Bromacil During the Early 1970's. . .	3
5-1	Mutagenicity Testing of Bromacil.	13

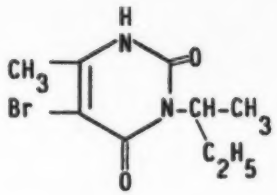
LIST OF ABBREVIATIONS

ADI	Acceptable daily intake
a.i.	Active ingredient
BCF	Bioconcentration factor
bw	Body weight
CNS	Central nervous system
LC_{50}	Concentration lethal to 50% of recipients
LD_{50}	Dose lethal to 50% of recipients
NOAEL	No-observed-adverse-effect level
ppm	Parts per million
STEL	Short term exposure limit
TLV	Threshold limit value
TLV-TWA	Threshold limit value-time-weighted average

1. INTRODUCTION

1.1. STRUCTURE AND CAS NUMBER

Bromacil is the common name for 5-bromo-3-sec-butyl-6-methyluracil. It is also known as 5-bromo-6-methyl-3-(1-methylpropyl)-2,4-(1H,3H)-pyrimidinedione. This herbicide was introduced in the market under the code number "DuPont Herbicide 976." It was also marketed under the tradenames "Hyvar" and "Hivor" (Sanborn et al., 1977; BCPC, 1977). The structure of bromacil is given below:



Molecular formula: $C_9H_{13}BrN_2O_2$

Molecular weight: 261.1

The Chemical Abstract Service (CAS) Registry number for this compound is 314-40-9.

1.2. PHYSICAL AND CHEMICAL PROPERTIES

Bromacil is a white crystalline solid and is used as a nonselective inhibitor of photosynthesis. It is mainly absorbed through the roots and is recommended for general weed control on noncrop land (BCPC, 1977). Some of the physical properties of bromacil are given below (BCPC, 1977; Hansch and Leo, 1981; Weber and Whitacre, 1982):

Melting Point:	158-159°C
Solubility in water at 25°C:	815 mg/ℓ
Vapor pressure at 100°C:	8×10^{-4} mm of Hg
pK_a($-\log_{10}$ of dissociation constant):	9.1
log octanol/water partition coefficient:	2.02

The compound is moderately soluble in strong aqueous bases, in acetone and ethanol. It slowly sublimes at temperatures just below its melting point and decomposes in the presence of strong acids (BCPC, 1977).

1.3. PRODUCTION DATA

Bromacil is prepared by the bromination of 3-sec-butyl-6-methyuracil (BCPC, 1977). Bromacil is produced by DuPont Co., Inc. at La Porte, Texas (SRI, 1983). The present U.S. production data are unavailable, but in 1972 the United States produced 4 million pounds of bromacil (Von Rumker et al., 1974).

1.4. USAGE DATA

Bromacil is widely used for the control of annual and perennial weeds including grasses and broadleaf weeds on non-cropland or on established citrus plantations (Acher and Dunkelblum, 1979; Acher and Saltzman, 1980; Jordan and Clerx, 1981). Although more recent usage data are unavailable, the average annual usage of bromacil by different sectors of the economy during the early 1970's is shown in Table 1-1.

TABLE 1-1

Average Annual Usage of Bromacil During the Early 1970's*

User	Quantity Used (millions of pounds)
Industrial/commercial	2.3
Government	0.3
Agricultural	0.4
Home and Garden	0
Export	1.0
Total	4.0

*Source: Von Rumker et al., 1974

2. ENVIRONMENTAL FATE AND TRANSPORT

Few experimental data are available regarding the environmental fate and transport of bromacil in the atmosphere. While the actual probability of chemical or photochemical reactions of bromacil in the atmosphere has not been investigated, the fate of bromacil in the air is likely to be determined by its ability to undergo direct photodecomposition or to react with O_3, NO_x and free radicals (e.g., RO•, O• and RO_2•). Judging from the lack of photoreactivity of this compound in aquatic media (Moilanen and Crosby, 1974) unless natural sensitizers such as humic acids or chlorophyll are present (Acher and Saltzman, 1980), it is unlikely that bromacil will undergo significant photoreaction in the troposphere.

In the atmosphere, bromacil appears likely to be sorbed on particulates based on its physical adsorption on soils (Rhodes et al., 1970). Both wet and dry precipitation are likely to remove the particulate-sorbed bromacil from the atmosphere. The distance this compound is transported in the atmosphere will be determined by the size of the particulate matter, with smaller particles having less tendency for dry deposition.

Photochemical reactions, hydrolytic reactions and free radical reactions are the three classes that may determine the fate of this chemical in aquatic media. Of these three possible classes, only photochemical reactions in aquatic media have been studied. Kearney et al. (1969) reported the complete decomposition of a 1 ppm aqueous solution of bromacil in 10 minutes when exposed to UV light at 254 nm, although a 10 ppm solution was more resistant to photolysis. However, experiments done under simulated natural conditions or under direct outdoor sunlight showed that bromacil was stable toward sunlight irradiation (Moilanen and Crosby, 1974). About 96% remained unchanged after irradiation of a 10 ppm solution in a photoreactor for 6

days. Only 2.2% of the main photoproduct (i.e., 5-bromo-6-methyluracil) was recovered. However, the presence of natural sensitizers (i.e., riboflavin, methylene blue, chlorophyll and humic acid) may greatly enhance the photodecomposition of bromacil in aquatic media under exposure to solar radiation (Acher and Saltzman, 1980). This sensitized photodecomposition is dependent on the pH of aquatic media. For example, the half-lives of aquatic bromacil were 45 minutes and 430 minutes at pH 9.2 and 6.8, respectively, in the presence of 2-5 ppm methylene blue sensitizer. With 20 ppm humic acids (present in natural aquatic media) as sensitizers, the half-lives of bromacil ranged from 225 minutes to 563 minutes at a pH of 9.2. The major products of this sensitized photodecomposition were identified as diastereoisomers of 3-sec-butyl-5-acetyl-5-hydroxyhydantoin (Acher and Dunkelblum, 1979). The sensitized photodecomposition reaction was also found to proceed at a fast rate in frozen aqueous solution (at -2 to -10°C). For example, the half-life of bromacil decomposition with rose bengal sensitizer was ~90 minutes at a pH of 9.1 and temperature of -2 to 10°C. The photodecomposition reaction remained substantial even when the frozen samples were covered with ice blocks of up to 11 cm thickness (Acher, 1982).

Although the rates of biodegradation of bromacil in aquatic media have not been determined, based on its biodegradability in soils (Zimdahl et al., 1970; Zandvoort et al., 1980) it is possible that biodegradation may play a significant role in determining the fate of bromacil in this media.

The two likely processes that may determine the transport characteristics of bromacil in aquatic media are sorption and volatilization. The volatilization rate data for bromacil from aquatic media are unavailable.

Based on its relatively high water solubility (815 mg/ℓ at 25°C) and low vapor pressure ($8x10^{-4}$ mm of Hg at 100°C), it is unlikely that significant volatilization of this compound will take place. (Extrapolating vapor pressure to 25°C, Henry's Constant at that temperature equals ~$2.2x10^{-9}$ atm $mmole^{-1}$, leading to an estimated volatilization half-life of ~40 years for a river of 100 cm average depth.) The adsorption of bromacil from aqueous solution onto some mineral surfaces was studied by Haque and Coshow (1971). For most of the surfaces, the adsorption was a physical process or Van der Waal's type adsorption. However, for surfaces that contain available protons (i.e., humic acid) some hydrogen bonding may take place. Thus, the adsorption was weak for montmorillonite and kaolinite but stronger for humic substances. Since surface water may contain humic substances, bromacil is likely to be adsorbed on these substances with subsequent partial precipitation to the sediment.

No experimental data on the bioconcentration of this chemical by aquatic organisms are available. From the binary regression equations of Kenaga (1980) a BCF of 3-14 can be derived based on water solubility and organic carbon adsorption. These latter values indicate that this compound is not expected to be significantly bioaccumulated in aquatic organisms.

The fate and transport of bromacil in soil has been studied more extensively, although none of the principal chemical reactions that may be responsible for the degradation of this chemical from soils (e.g., hydrolysis, radical oxidation and photochemical reaction) have been studied specifically.

Available data indicate that soil microorganisms may significantly biodegrade bromacil in soil. For example, in field experiments, Gardiner et al. (1969a) found a half-life of ~6 months for bromacil in soils. Jolliffe

et al. (1967) found a degradation of 31-65% in 6 soils after incubation for 6 months under laboratory conditions. Zimdahl et al. (1970) determined a half-life of 4-5 months for bromacil in nonsterilized soils. No degradation was observed in sterile soil (Zandvoort et al., 1980).

The two important processes that may control the transport of bromacil in soils are volatilization and leaching. The volatilization of bromacil from soils is likely to be an insignificant process (Zandvoort et al., 1980). The leaching of bromacil from soils is dependent on the soil absorption coefficient and its water solubility. The adsorption of bromacil in soils was studied by Rhodes et al. (1970). Since the adsorption of bromacil in soil is generally a weak physical process (Van der Waal's adsorption) and the solubility of this compound is relatively high, significant leaching of the compound from soil has been observed (Weber and Whitacre, 1982; Zandvoort et al., 1980; Paulo et al., 1979). For example, Weber and Whitacre (1982) found 10.4% of the applied bromacil on Lakeland soil leached into 25-30 cm soil depth after 30 days. Zandvoort et al. (1980) found bromacil concentration to be highest in the 10-20 cm layer of soil. Within 2 years, the compound penetrated down to a depth of 100 cm. Hebb and Wheeler (1978) found that leaching of bromacil into groundwater can occur under extreme conditions, particularly sandy soil with low organic matter, plentiful rainfall and a water table of <6 m. Field experiments also have shown that bromacil had a longer persistence in sandy soil than in clay soil and bromacil disappeared first from the upper soil layer and then from lower layers (Stecko, 1971).

The fate of ^{14}C-labeled bromacil in a terrestrial laboratory ecosystem was studied by Gile et al. (1980). After application of 0.28 kg/ha to the laboratory ecosystem, the ^{14}C levels in different compartments were

determined after 22 days. Of the total applied radioactivity, 0.3, 32, 34, 34 and 0% were found in animal population, air, soil, plants and groundwater, respectively. The authors stated that, because the ^{14}C label was in the second carbon position, which is readily converted to CO_2, the ^{14}C in air probably reflected CO_2 rather than parent compound or other volatile metabolites. The radioactivity in the soil was found primarily in the upper 6 cm, indicating that bromacil was relatively immobile under the conditions of this study.

3. EXPOSURE

Very few monitoring data for bromacil in different media are available. STORET contains two observations for this herbicide in Tombigbee River, Michigan. Water samples taken in 1980 from two outfalls of Hooker Chemical Company, Columbus, Michigan, into Tombigbee River showed bromacil concentrations of 370 and 32,000 µg/ℓ. No report of bromacil in drinking waters, however, could be found. The groundwater of Okinawa, Japan, was monitored for bromacil after soil application of the herbicide and none was detected (Tanto, 1977). Similarly, 30-50 ppm bromacil was detected in Ponderosa pine foliage near a road that had been sprayed with the herbicide 9 months earlier (Ferenbaugh et al., 1981). Although there are indications that some absorption of bromacil from soil to plant roots and a subsequent translocation to leaves may take place (Jordan and Clerx, 1981), no food residue data for this herbicide are available. Bromacil residue in Florida citrus soils was monitored 1 year after application. Only a small amount of bromacil (<0.04-1.10 ppm) was detected in soils. Continuous applications at recommended rates and frequencies may result in a maximum soil bromacil level of 3.9% of the total application (Tucker, 1978).

4. COMPOUND DISPOSITION AND PHARMACOKINETICS

4.1. ABSORPTION

No studies examining the absorption of bromacil were found in the available literature; however, it can be inferred from the metabolism study of Gardiner et al. (1969b) in rats and the excretion study of Gutenmann and Lisk (1970) in cows that bromacil is absorbed from the gastrointestinal tract of both species of animals following oral administration in the diet.

4.2. DISTRIBUTION

No studies examining the distribution of bromacil were found in the available literature; however, it can be inferred from the excretion study of Gutenmann and Lisk (1970) that bromacil is distributed in and excreted by the mammary glands of cows following oral administration in the diet.

4.3. METABOLISM

Gardiner et al. (1969b) administered 1250 ppm of bromacil in the diet of Charles River-CD rats for 1 month. Total daily urine samples were collected during the last 2 weeks of treatment. In addition to the intact compound, the following metabolites were recovered in the urine: 5-bromo-3-sec-butyl-6-hydroxymethyluracil (I), 5-bromo-3-(2-hydroxy-1-methylpropyl)-6-methyluracil (II), 5-bromo-3-(2-hydroxy-1-methylpropyl)-6-hydroxymethyluracil (III), 3-sec-butyl-6-hydroxymethyluracil (IV), 5-bromo-3-(3-hydroxy-1-methylpropyl)-6-methyluracil (V), 3-sec-butyl-6-methyluracil (VI), and an unidentified bromine-containing compound (VII, molecular weight of 339). 5-Bromouracil was not detected as a metabolite of bromacil. Gardiner et al. (1969b) reported the following estimated concentrations in the urine: bromacil, 20 ppm; metabolite I, 21 ppm; metabolite II, 7 ppm; metabolites III and V (combined concentration), 4 ppm; metabolite IV, 4 ppm; metabolite VI, 0.3 ppm; and metabolite VII, <10 ppm. The formation of metabolites

occurred by oxidation of the 6-methyl group, oxidation of the 3-sec-butyl group, or debromination of the 5-bromo group, and by combinations of these three reactions. No conclusions were offered by the authors as to the order of metabolite formation. Gardiner et al. (1969b) observed evidence of substantial glucuronide and sulfate conjugation of 5-bromo-3-sec-butyl-6-hydroxymethyluracil (metabolite I) in the urine of treated animals and a lesser degree of similar conjugation of the other bromacil metabolites (II, III, IV, V, VI and VII); little, if any, bromacil was present as glucuronide or sulfate conjugates in the urine of treated animals.

In in vitro assays, Gutenmann and Lisk (1970) did not observe any metabolism of bromacil when the compound was incubated with fresh rumen fluid for 7 hours or with a 10,000 xg supernatant of homogenized cow liver for 1 hour.

4.4. EXCRETION

Gutenmann and Lisk (1970) administered 5 or 30 ppm of bromacil in the feed of lactating Holstein dairy cows for 4 days. Urine, feces and milk samples were collected during the 4 days of administration and for 6 days subsequent to treatment for the cow ingesting 5 ppm of bromacil, while only milk samples were collected during the same time period for the cow ingesting 30 ppm of bromacil. The intact compound was excreted in the milk of both cows at a concentration of 0.019 ppm at the lower dose level and 0.13 ppm at the higher dose level. No bromacil was detected in the urine or feces of the cow that was administered 5 ppm.

Qualitative evidence of excretion of bromacil and its metabolites in the urine of rats administered 1250 ppm of bromacil in the diet for 1 month can be obtained from the metabolism study of Gardiner et al. (1969b), but quantitative results were not presented in this study.

5. EFFECTS

5.1. CARCINOGENICITY

Epidemiology studies are not available that evaluate bromacil's possible carcinogenicity. In chronic animal studies by Sherman and Kaplan (1975) and Sherman (1968), weanling Charles River-CD rats (36 males and 36 females per dose level) were administered dietary concentrations of 0, 50, 250 or 1250 ppm of bromacil ad libitum for 2 years. At the 1250 ppm dose level, thyroid changes occurred that were characterized by a slightly increased incidence of focal light cell hyperplasia and focal follicular cell hyperplasia. In addition, a follicular cell adenoma was observed in one female rat ingesting 1250 ppm of bromacil. No further details concerning tumor incidence in treated or control animals were reported. No pathological changes suggestive of carcinogenicity were noted in Charles River-CD rats or beagle dogs administered similar dose levels of bromacil for 90 days or 2 years, respectively, although these lengths of administration are rather short consideration the lifespan of dogs (Sherman and Kaplan, 1975; Sherman, 1968).

5.2. MUTAGENICITY

The mutagenicity of bromacil has been tested in various bacteria, yeast, Drosophila, mammalian and plant assays. These mutagenicity tests are summarized in Table 5-1.

Both positive and negative results have been obtained with bromacil in mutagenicity assays of reverse mutation in Salmonella typhimurium (Gopalan and Njagi, 1981; Njagi and Gopalan, 1980; Simmon et al., 1976; Andersen et al., 1972) and in rec-assays of repair deficient and proficient strains of Bacillus subtilis and Escherichia coli (Shirasu et al., 1976; Simmon et al., 1976). Siebert and Lemperle (1974) obtained negative results for bromacil in a mitotic gene conversion assay with Saccharomyces cerevisiae, while

TABLE 5-1

Mutagenicity Testing of Bromacil

Assay	Indicator Organism	Application	Concentration or Dose	Activation System	Response	Comment	Reference
Reverse mutation	Salmonella typhimurium strains(s) NR	NR	NR	None	+	NC	Gopalan and Njagi, 1981; Njagi and Gopalan, 1980
Reverse mutation	S. typhimurium 5 strains NR	NR	NR	±S9	+	The abstract of this study only indicated a positive response, and did not differentiate between responses obtained with or without the mammalian metabolic activation system.	Simmon et al., 1976
Reverse mutation	S. typhimurium 8 strains NR	spot test	~1-5 µℓ	None	-	NC	Andersen et al., 1972
Rec-assay	Bacillus subtilis H17 Rec+ M45 Rec-	spot test	NR	None	- -	NC	Shirasu et al., 1976
Rec-assay	B. subtilis repair deficient and proficient strains	NR	NR	None	+	NC	Simmon et al., 1976
Rec-assay	Escherichia coli repair deficient and proficient strains	NR	NR	±S9	+	The abstract of this study only indicated a positive response, and did not differentiate between responses obtained with or without the mammalian metabolic activation system.	Simmon et al., 1976
Mitotic gene conversion	Saccharomyces cerevisiae diploid strain	cell culture	1000 ppm	NR	-	NC	Siebert and Lemperle, 1974

TABLE 5-1 (cont.)

Assay	Indicator Organism	Application	Concentration or Dose	Activation System	Response	Comment	Reference
Mitotic recombination	S. cerevisiae diploid strain	NR	NR	±S9	+	The abstract of this study only indicated a positive response, and did not differentiate between responses obtained with or without the mammalian metabolic activation system.	Simmon et al., 1976
Mitotic recombination	S. cerevisiae D3	NR	NR	±S9	-	NC	Riccio et al., 1981
Mitotic crossing-over	S. cerevisiae D7	NR	NR	±S9	-	NC	Riccio et al., 1981
Mitotic gene conversion	S. cerevisiae D7	NR	NR	±S9	-	NC	Riccio et al., 1981
Reverse mutation	S. cerevisiae D7	NR	NR	±S9	-	NC	Riccio et al., 1981
Reverse mutation	bacteriophage T_4	bromacil added to test tube; plaque formation, E. coli	50 µg	None	-	NC	Andersen et al., 1972
Reverse mutation	rII mutants of bacteriophage T_4; bacteriophage AP72 bacteriophage N17	bromacil added to test tube; plaque formation, E. coli	500 µg	None	- -	NC	Andersen et al., 1972
Sex-linked recessive lethal	Drosophila melanogaster	feeding, with possible contact and inhalation exposures	NR	None	+,+[a]	NC	Valencia, 1981
Sex-linked recessive lethal	D. melanogaster	NR	NR	None	-	NC	Gopalan and Njagi, 1981
Dominant lethal	D. melanogaster	NR	NR	None	+	Exposure to bromacil did not affect chromosomal breakage or loss; however, the exposure did significantly increase the frequency of non-disjunction and loss.	Murnik, 1976

TABLE 5-1 (cont.)

Assay	Indicator Organism	Application	Concentration or Dose	Activation System	Response	Comment	Reference
Dominant lethal	ICR/Ha Swiss mice	i.p. injection	150 mg/kg x 1	None	+,-[b]	NC	Epstein et al., 1972
Dominant lethal	ICR/Ha Swiss mice	gavage	750 or 1000 mg/kg x 5	None	+,-[b]	NC	Epstein et al., 1972
Dominant lethal	mice (strain NR)	diet	3 dose levels (NR)	None	-	NC	Jorgenson et al., 1976
Chromosomal aberrations	Hordeum vulgare (barley seeds)	seeds were soaked in bromacil solutions	500, 1000 or 1500 ppm for 6, 12 and 24 hours at each dose level	None	+	Increased chromosomal aberrations were observed in root tips of barley seedlings as the exposure time at each dose level increased.	Wuu and Grant, 1966
Chromosomal aberrations	H. vulgare (barley seeds)	seeds were soaked in bromacil solutions	1000 ppm for 12 hours	None	+	NC	Wuu and Grant, 1967
Chromosomal aberrations	H. vulgare (barley seeds)	spray applied to plants	500 ppm	None	+	NC	Wuu and Grant, 1967
Chromosomal aberrations	Solanum surattense	NR	300 ppm	None	+	NC	Bakale and Kolhe, 1982
Chromosomal aberrations	Vicia faba	NR	NR	None	+	NC	Gopalan and Njagi, 1981

[a]Bromacil was determined to be a weak mutagen in the sex-linked recessive lethal assay in Drosophila melanogaster.

[b]This was not a true positive mutagenic response, as the number of early fetal deaths and/or preimplantation losses were greater than control values but not statistically significant.

NR = Not reported, NC = No comment, i.p. = intraperitoneal

Simmon et al. (1976) noted positive results of bromacil in a mitotic recombination assay with S. cerevisiae. Riccio et al. (1981) obtained negative results with S. cerevisiae strain D3 in the mitotic recombination assay and with S. cerevisiae strain D7 in the mitotic crossing-over, mitotic gene conversion, and reverse mutation assays. Andersen et al. (1972) reported that bromacil had no mutagenic activity in reverse mutation assays with either bacteriophage T_4 or two rII mutants of bacteriophage T_4 (bacteriophage AP72 and N17).

In sex-linked recessive lethal assays with Drosophila melanogaster, Valencia (1981) reported that bromacil was a weak mutagen following oral administration, while Gopalan and Njagi (1981) reported a negative mutagenic response for bromacil (route of administration not reported). Murnik (1976) observed a positive mutagenic response for bromacil in the dominant lethal assay in D. melanogaster.

Epstein et al. (1972) administered bromacil in a single intraperitoneal injection of 150 mg/kg or 5 gavage doses of 750 or 1000 mg/kg to male ICR/Ha Swiss mice. Suggestive evidence of dominant lethal effects was observed after mating of all groups of treated males with untreated females; the number of early fetal deaths and/or preimplantation losses were greater than corresponding control values but were not statistically significantly different. Following oral administration of bromacil in the diet of male mice (strain and dose levels not reported), Jorgenson et al. (1976) did not observe an increased incidence of dominant lethal effects.

Chromosomal aberrations in three species of plants, Hordeum vulgare (Wuu and Grant, 1966, 1967), Solanum surattense (Bakale and Kolhe, 1982), and Vicia faba (Gopalan and Njagi, 1981), were induced by application of various concentrations of bromacil.

The information currently available is inadequate to make a definitive conclusion whether or not bromacil is mutagenic. Many of the studies mentioned in the document are preliminary and are in the form of abstracts of papers presented at scientific meetings and do not provide data for analysis: some studies contradict each other. The only system in which bromacil was found to induce chromosomal aberrations was the plant system. However, the relevance of plant studies to human health has not yet been determined.

5.3. TERATOGENICITY

Groups of 10 pregnant Sprague-Dawley rats were exposed to bromacil aerosols at concentrations of 38, 78 or 165 mg/m^3 for 2 hours/day on days 7 through 14 of gestation (Newell and Dilley, 1978; Dilley et al., 1977). Both air-treated controls and DMSO-exposed controls were used. Treatment with bromacil at any of the three dose levels did not induce maternal toxicity. The treated animals were killed on day 20 of gestation, at which time both dams and fetuses were examined for gross pathological changes. The incidence of terata was not increased by treatment with the levels of bromacil tested. At the 165 mg/m^3 dose level, a slightly higher incidence of resorptions was observed as compared to the two lower dose groups; however, both of the control groups (air and DMSO) had resorption rates that were slightly higher than historical control values and higher than any of the exposed groups. Dose-related decreases in fetal weight and caudal ossification were significant ($p<0.01$) at the dose levels tested, while the incidence of sternal ossification and supernumerary ribs was similar to control values for all three dose levels.

Sherman and Kaplan (1975) and Sherman (1968) administered 0, 50 or 250 ppm of bromacil in the diet to pregnant New Zealand white rabbits on days 8 through 16 of gestation. No gross anomalies in bone structure were observed in the fetuses obtained by Caesarean section on day 29 or 30 of gestation or in those obtained by normal parturition.

5.4. OTHER REPRODUCTIVE EFFECTS

In a 3-generation reproduction study, Sherman and Kaplan (1975) and Sherman (1968) administered 250 ppm of bromacil in the diet to 12 male and 12 female weanling Charles River-CD rats (parental generation) for 12 weeks. The first and second generations were subsequently administered 250 ppm of bromacil in the diet for 110 days. No changes were noted in the various reproduction or lactation indices that were measured. Neither changes in weights nor treatment-related gross or microscopic pathological changes in tissues were observed in the third generation weanling pups.

5.5. CHRONIC AND SUBCHRONIC TOXICITY

In a chronic dietary study, groups of 36 male and 36 female weanling Charles River-CD rats per dose level were administered 0, 50, 250 or 1250 ppm of bromacil ad libitum for 2 years (Sherman and Kaplan, 1975; Sherman, 1968). No changes were observed in treated animals compared with controls for hematological, biochemical or urine analyses or in organ weight changes or tibia length. At the highest dose level, thyroid changes occurred that were characterized by a slightly increased incidence of focal light cell hyperplasia and focal follicular cell hyperplasia. Follicular cell adenoma was noted in one female rat ingesting 1250 ppm of bromacil.

In a subchronic dietary study by the same investigators (Sherman and Kaplan, 1975; Sherman, 1968), groups of 10 male and 10 female Charles River-CD rats per dose level were administered 0, 50, 500 or 2500 ppm of

bromacil for 90 days. In the absence of any signs of toxicity after 10 weeks of administration, half of the rats at the 2500 ppm level were fed 6000 ppm for 1 week followed by 7200 ppm for 2 weeks. No deaths or changes in urine or hematological indices were observed at any dose level. Upon histopathological examination, animals from the highest dose level were observed to have changes in the thyroid that the authors considered suggestive of increased glandular activity; enlargement of centrolobular hepatocytes was also observed at the highest dose level.

Sherman and Kaplan (1975) and Sherman (1968) also administered 0, 50, 250 or 1250 ppm of bromacil in the diet to beagle dogs (3 males and 3 females per dose level) for 2 years. The highest dose level was achieved in sequential steps of 250 ppm for 3 days, 750 ppm for 5 days, and 1250 ppm for the remainder of the 2-year treatment period. At the 1250 ppm dose level, decreased body weights without accompanying decreased food intake was noted. No changes in hematologic, urinalysis, biochemical or pathologic parameters were observed at any dose level when compared to controls.

5.6. OTHER RELEVANT INFORMATION

Bromacil has a low order of toxicity when administered to humans or experimental animals. Bromacil is used as an antidepressant formulation for humans at a dose of 50 mg in a gelatin capsule (Sankyo Co., Ltd., 1982). The oral LD_{50}s of bromacil for mice, rats and dogs are 3040, 5200 and >5000 mg/kg, respectively (Reinhardt and Brittelli, 1981).

Sherman and Kaplan (1975) and Sherman (1968) have assessed the acute oral, dermal and inhalation toxicity of bromacil. The oral LD_{50} of bromacil in Charles River-CD rats was 5200 mg/kg; at this dose level, surviving animals were observed to have rapid respiration, discomfort and initial weight loss. The dermal LD_{50} of bromacil in albino rabbits was >5000 mg/kg for a 24-hour exposure to a 70% aqueous paste followed by a 13-day

observation period. No clinical signs of toxicity or gross pathological changes resulted from dermal exposure to levels ≤5000 mg/kg. Mild temporary conjunctivitis without corneal damage was observed in the eyes of rabbits exposed to either 10 mg of bromacil (dry powder) or 0.1 mℓ of a 10% suspension of bromacil in mineral oil. An LC_{50} for bromacil of >4.8 mg/ℓ was observed in Charles River-CD rats inhaling bromacil vapors at a concentration of 2.1 or 4.8 mg/ℓ for 4 hours, followed by a 14-day observation period. Exposed animals were noted to have rapid, deep respiration, and ruffled fur.

In a short-term oral toxicity study, Sherman and Kaplan (1975) and Sherman (1968) treated male Charles River-CD rats with bromacil via gastric intubation at levels of 0, 650, 1035 or 1500 mg/kg/day, 5 times/week, for 2 weeks. The surviving treated animals were subsequently observed for 14 days. The 4 of 6 animals that died after 5 doses of 1500 mg/kg/day and the 1 of 6 animals that died after 4 doses of 1035 mg/kg/day were observed to have gastrointestinal (poorly formed feces) and CNS (incoordination and salivation) disturbances, as well as focal liver cell hypertrophy and transient hyperplasia. At the 650 mg/kg/day dose level, 6 of 6 animals survived 10 doses and had similar but less severe pathological changes as those observed at the two higher dose levels.

Palmer (1965) fed Delaine-Merino sheep either 100 mg bromacil/kg bw for 11 treatments or 250 mg bromacil/kg bw for five treatments. At the 100 mg/kg level, the sheep were unaffected with the exception of a decreased body weight. At the 250 mg/kg level, the sheep had tympany and stilted gait within 4 hours after administration of the initial dose that progressed in severity with subsequent doses; marked lameness of one leg and incoordination also were noted. The symptoms were transient, returning to normal after discontinuation of treatment.

6. AQUATIC TOXICITY

6.1. ACUTE TOXICITY

The only available information concerning acute toxicity of bromacil to aquatic animals was provided by Schneider (1979), who reported that 100 ppm of a bromacil formulation (5.4% a.i.) was not lethal to bluegill sunfish, Lepomis macrochirus, during a 96-hour exposure period.

6.2. CHRONIC TOXICITY

Pertinent data regarding chronic effects of bromacil were not located in the available literature.

6.3. PLANT EFFECTS

Kratky and Warren (1971) reported that 18-36 hours of incubation in 1 and 10 ppm of technical-grade bromacil produced >50% growth inhibition of the alga, Chlorella pyrenoidosa, as measured by chlorophyll content. In field studies, Taylor and Burrows (1968) reported that application of a bromacil formulation at 5 lbs a.i./acre resulted in >99% elimination of the saltmarsh grass, Spartina townsendii, in test plots in an English estuary.

6.4. RESIDUES

Pertinent data regarding bromacil residues were not located in the available literature.

6.5. OTHER RELEVANT INFORMATION

Pertinent data regarding other relevant information on bromacil were not located in the available literature.

7. EXISTING GUIDELINES AND STANDARDS

7.1. HUMAN

A tolerance of 0.1 ppm for bromacil residues in or on citrus fruits and pineapples has been established under the Federal Food, Drug, and Cosmetic Act (32 FR 4352).

The American Conference of Governmental Industrial Hygienists (ACGIH, 1980) has set a TLV-TWA of 1 ppm and a STEL of 2 ppm for bromacil.

7.2. AQUATIC

Guidelines or standards for the protection of aquatic organisms from the toxic effects of bromacil have not been derived.

8. RISK ASSESSMENT

There is no evidence that bromacil induces neoplasia in experimental animals. In a chronic dietary study with bromacil, focal light cell hyperplasia, focal follicular cell hyperplasia, and a single incidence of follicular cell adenoma were observed in rats (Sherman and Kaplan, 1975; Sherman, 1968). Positive results have been obtained for bromacil in some *in vitro* mutagenicity assays with bacteria (Gopalan and Njagi, 1981; Njagi and Gopalan, 1980; Simmon et al., 1976) and yeast (Simmon et al., 1976), and in *in vivo* tests with *Drosophila melanogaster* (Valencia, 1981; Murnik, 1976). Exposure to bromacil aerosols induced fetotoxicity but not terata in the fetuses nor maternal toxicity in exposed rats (Newell and Dilley, 1978; Dilley et al., 1977). No gross anomalies in bone structure were observed in the fetuses of New Zealand white rabbits administered dietary concentrations of bromacil (Sherman and Kaplan, 1975; Sherman, 1968). Neither gross or microscopic histological changes nor alterations in various reproduction or lactation indices were observed in rats fed dietary concentrations of bromacil over 3 generations (Sherman and Kaplan, 1965; Sherman, 1968).

The chronic dietary study of Sherman and Kaplan (1975) and Sherman (1968) can be used for quantitative risk assessment for bromacil. Both sexes of Charles River-CD rats and beagle dogs were administered dietary concentrations of 0, 50, 250 or 1250 ppm of bromacil *ad libitum* for 2 years (Sherman and Kaplan, 1975; Sherman, 1968). At the 1250 ppm dose level, rats were observed to have thyroid changes that were characterized by a slightly increased incidence of focal light cell hyperplasia and focal follicular cell hyperplasia, while follicular cell adenoma was noted in one female; dogs at this dose level were observed to have decreased body weights without accompanying decreased food intake. A NOAEL may be defined as 250 ppm for

both rats and dogs, as no treatment-related effects were seen in either species at this dose level. It is more appropriate to derive an ADI value from the NOAEL for rats rather than for dogs, as 72 rats/dose level as compared to 6 dogs/dose level were used; also, there are supporting data for rats from the previously discussed teratogenicity and reproduction studies, in which a similar dietary dose of 250 ppm of bromacil had no effect on production of terata or on reproductive capacity, and from a 90-day subchronic dietary study (Sherman and Kaplan, 1975; Sherman, 1968).

Using the NOAEL of 250 ppm in rats, derived from the studies of Sherman and Kaplan (1975) and Sherman (1968), an ADI value can be derived. In lieu of the absence of food consumption data, the assumption that a rat consumes a daily amount of food equivalent to 5% of its body weight must be made. Using this assumption, an equivalent dose of 12.5 mg/kg/day can be calculated. An ADI value of 8.75 mg/day for a 70 kg human can be calculated by multiplying the animal dose by an assumed human body weight of 70 kg and by dividing by an uncertainty factor of 100 to convert from experimental animal data to humans, and to protect the more sensitive individuals of a population.

For comparison, an ADI value for bromacil can be calculated for inhalation exposure using the TLV of 1 ppm (equivalent to 10.7 mg/m^3). The chronic dietary studies of Sherman and Kaplan (1975) and Sherman (1968) were among the data used as the basis for establishing this TLV. Several assumptions were made, including an inhalation absorption efficiency of 50%, a human breathing volume of 10 m^3/8-hour work day, and an occupational exposure of 5 days/week, 8 hours/day. An equivalent dose of 38.2 mg/day is calculated by multiplying the TLV by the assumed human breathing volume, 5/7

to expand the dose over 7 days, and the assumed inhalation absorption efficiency. Applying an uncertainty factor of 10 to protect the more sensitive individuals of a population results in an ADI of 3.82 mg/day, or 0.055 mg/kg/day, assuming a body weight of 70 kg.

Statements concerning available literature in this document refer to published, quotable sources and are in no way meant to imply that confidential data, which this document could not address, are not in existence. These data, which are considered Confidential Business Information (CBI), are available in summary form as a CBI Appendix that can be accessed by individuals with appropriate clearance. Conclusions from the CBI Appendix regarding risk assessment, however, can be presented in this chapter.

The CBI Appendix to this document reviews other animal studies that indicate that bromacil is carcinogenic to mice. A q_1^* for humans of 6.38×10^{-2} $(mg/kg/day)^{-1}$ was calculated from dose-response data for hepatocellular carcinoma and adenoma in male mice fed bromacil in the diet. The q_1^* value was calculated using the linearized multistage model developed by Kenneth Crump and adopted by the U.S. EPA (Federal Register, 1980). The conversion factor used in the calculation of this q_1^* value for humans (assuming 70 kg bw) from animal data is the cube root of the body weight ratio (Federal Register, 1980).

9. REFERENCES

ACGIH (American Conference of Governmental Industrial Hygienists). 1980. Bromacil. TLVs: Documentation of the Threshold Limit Values. 4th ed. (Includes Supplemental Documentation, 1981). Cincinnati, OH, 486 p.

Acher, A.J. 1982. The fate of organic pollutants in frozen waters: Sunlight photodecomposition of uracil herbicides in frozen aqueous solutions. Water Res. 16(4): 405-410.

Acher, A.J. and E. Dunkelblum. 1979. Identification of sensitized photooxidation products of bromacil in water. J. Agric. Food Chem. 27(6): 1164-1167.

Acher, A.J. and S. Saltzman. 1980. Dyesensitized photooxidation of bromacil in water. J. Environ. Qual. 9(2): 190-194.

Andersen, K.J., E.G. Leighty and M.T. Takahashi. 1972. Evaluation of herbicides for possible mutagenic properties. J. Agric. Food Chem. 20: 649-656.

Bakale, V.L. and R.L. Kolhe. 1982. Effect of herbicides on meiosis in Solanum surattense Burm. F. Biovigyanam. 8(1): 7-9. (Taken from Chem. Abstr. 97:176840R)

BCPC (British Crop Protection Council). 1977. Pesticide Manual. 5th ed. H. Martin and C.R. Worthing, Ed. BCPC Publications, England. p. 48.

Dilley, J.V., N. Chernoff, D. Kay, N. Winslow and G.W. Newell. 1977. Inhalation teratology studies of five chemicals in rats. Toxicol. Appl. Pharmacol. 41: 196.

Epstein, S.S., E. Arnold, J. Andrea, W. Bass and Y. Bishop. 1972. Detection of chemical mutagens by the dominant lethal assay in the mouse. Toxicol. Appl. Pharmacol. 23: 288-325.

Federal Register. 1980. Methodology Used in the Preparation of Health Effects Assessment Chapters of the Consent Decree Water Criteria Documents. Vol. 45. p. 79347-79357.

Ferenbaugh, R.W., W.D. Spall and D.M. Lacombe. 1981. Detection of bromacil herbicide in Ponderosa pine. Bull. Environ. Contam. Toxicol. 27: 268-273.

Gardiner, J.A., R.C. Rhodes, J.B. Adams, Jr. and E.J. Soboczinske. 1969a. Synthesis and studies with 2-C14 labeled bromacil and terbacil. J. Agric. Food Chem. 17: 980-986.

Gardiner, J.A., R.W. Reiser and H. Sherman. 1969b. Identification of the metabolites of bromacil in rat urine. J. Agric. Food Chem. 17(5): 967-973.

Gile, J.D., J.C. Collins and J.W. Gillett. 1980. Fate of selected herbicides in a terrestrial laboratory microcosm. Environ. Sci. Technol. 14(9): 1124-1128.

Gopalan, H.N.B. and G.D.E. Njagi. 1981. Mutagenicity testing of pesticides. Genetics. 97(S1): S44.

Gutenmann, W.H. and D.J. Lisk. 1970. Metabolism and excretion of Bromacil in milk of dairy cows. J. Agric. Food Chem. 18(1): 128-129.

Hansch, C. and A.J. Leo. 1981. Medchem Project. Issue No. 19. Pomona College, CA.

Haque, R.C. and W.R. Coshow. 1971. Adsorption of isocil and bromacil from aqueous solution onto some mineral surfaces. Environ. Sci. 5(2): 139-141.

Hebb, E.A. and W.B. Wheeler. 1978. Bromacil in Lakeland soil groundwater. J. Environ. Qual. 7(4): 598-601.

Johannsen, F.R., G.J. Levinskas, P.L. Wright and D.E. Gordon. 1977. Toxicological evaluation of Avadex and Avadex BW herbicides. Int. Congr. Toxicol. (1977): 3.

Jolliffe, V.A., B.E. Day, L.S. Jordan and J.D. Mann. 1967. Method of determining bromacil in soils and plant tissues. J. Agric. Food Chem. 15: 174-177.

Jordan, L.S. and W.A. Clerx. 1981. Accumulation and metabolism of bromacil in Pineapple sweet orange (Citrus sinensis) and Cleopatra mandarin (Citrus reticulata). Weed Sci. 29(1): 1-5.

Jorgenson, T.A., C.J. Rushbrook and G.W. Newell. 1976. In vivo mutagenesis investigations of ten commercial pesticides. Toxicol. Appl. Pharmacol. 37: 109.

Kearney, P.C., E.A. Woolson, J.R. Plimmer and A.R. Isensee. 1969. Decontamination of pesticides in soils. Res. Rev. 29: 137-149.

Kenaga, E.E. 1980. Predicted bioconcentration factors and soil sorption coefficients of pesticides and other chemicals. Ecotox. Environ. Safety. 4: 26-38.

Kratky, B.A. and G.F. Warren. 1971. Use of three simple, rapid bioassays on forty-two herbicides. Weed Res. 11(4): 257-262.

Moilanen, K.W. and D.G. Crosby. 1974. The photodecomposition of bromacil. Arch. Environ. Contam. Toxicol. 2: 3-8.

Murnik, M.R. 1976. Mutagenicity of widely used herbicides. Genetics. 83: S54.

Newell, G.W. and J.V. Dilley. 1978. Teratology and acute toxicology of selected chemical pesticides administered by inhalation. Prepared by SRI, Menlo Park, CA for U.S. EPA, HERL, RTP, NC. EPA 600/1-78-003.

Njagi, G.D.E. and H.N.B. Gopalan. 1980. Mutagenicity testing of some selected food preservatives, herbicides, and insecticides. Bangladesh J. Bot. 9(2): 141-146.

Palmer, J.S. 1965. Toxicity of methyluracil and substituted urea and phenol compounds to sheep. J. Am. Vet. Med. Assoc. 145: 787.

Paulo, E.M., L.H. Signori and R. Deuber. 1979. Leaching of metribuzin, oxadiazon and bromacil in two types of soils. Planta Daninha. 2(2): 111-115.

Reinhardt, C.F. and M.R. Brittelli. 1981. Heterocyclic and Miscellaneous Nitrogen Compounds. In: Patty's Industrial Hygiene and Toxicology, 3rd rev. ed., Vol. 2A, G.D. Clayton and F.E. Clayton, Ed. John Wiley and Sons, Inc., NY. p. 2671-2822.

Rhodes, R.C., I.J. Belasco and H.L. Pease. 1970. Determination of mobility and adsorption of agrichemicals on soils. J. Agric. Food Chem. 18(3): 524-528.

Riccio, E., G. Shepherd, A. Pomeroy, K. Mortelmans and M.D. Waters. 1981. Comparative studies between the S. cerevisiae D3 and D7 assays of eleven pesticides. Environ. Mutag. 3(3): 327.

Sanborn, J.R., B.M. Francis and R.L. Metcalf. 1977. The Degradation of Selected Pesticides in Soil: A Review of the Published Literature. MERL, U.S. EPA, Cincinnati, OH. EPA 600/9-77-022. p. 35-38.

Sankyo Co., Ltd. 1982. Antidepressant formulations containing bromacil. Japanese Patent No. 82, 42624. March 10, 1982. (Taken from Chem. Abstr. 97:011839j)

Schneider, B.A. 1979. Toxicology handbook mammalian and aquatic data. Book 1. Toxicology data. Off. Pest. Progr., U.S. EPA, Washington, DC. EPA 540/9-79-033A. NTIS PB 80-196876.

Sherman, H. 1968. Toxicity of bromacil, a substituted uracil. Toxicol. Appl. Pharmacol. 12: 313.

Sherman, H. and A. Kaplan. 1975. Toxicity studies with 5-bromo-3-sec-butyl-6-methyluracil. Toxicol. Appl. Pharmacol. 34: 189-196.

Shirasu, Y., M. Moriya, K. Kato, A. Furuhashi and T. Kada. 1976. Mutagenicity screening of pesticides in the microbial system. Mutat. Res. 40: 19-30.

Siebert, D. and E. Lemperle. 1974. Genetic effects of herbicides: Induction of mitotic gene conversion in Saccharomyces cerevisiae. Mutat. Res. 22: 111-120.

Simmon, V.F., D.C. Poole and G.W. Newell. 1976. In vitro mutagenic studies of twenty pesticides. Toxicol. Appl. Pharmacol. 37: 109.

SRI (Stanford Research Institute) International. 1983. 1983 Directory of Chemical Producers. United States of America. Menlo Park, CA. p. 774.

Stecko, V. 1971. Comparison of the persistence and the vertical movement of the soil-applied herbicides simazine and bromacil. Proc. Br. Weed Contr. Conf. 1: 303-306.

Tanto, M. 1977. Herbicide residues in soils and drinking water. Okinawaken Kogai Eisei Kenkyusho Ho. 10: 37-39.

Taylor, M.C. and E.M. Burrows. 1968. Chemical control of fertile Spartina townsendii on the Cheshire shore of the Dee estuary. I. Field trials on Spartina sward. Weed Res. 8(3): 170-184.

Tucker, D.P.H. 1978. Bromacil and diuron residue levels in Florida citrus soils. Pestic. Monit. J. 12(2): 47-50.

Valencia, R. 1981. Mutagenesis screening of pesticides 'Drosophila'. ISS EPA 600/1-81-017. NTIS PB 81-160848. 82 p.

Von Rumker, R., E.W. Lawless, A.F. Meiners, K.A. Lawrence, G.L. Kelso and F. Horay. 1974. Production, Distribution, Use, and Environmental Impact Potential of Selected Pesticides. Report prepared by Midwest Research Institute, Kansas City, MO. Prepared for Council on Environmental Quality, Washington, DC. NTIS PB-238795.

Weber, J.B. and D.M. Whitacre. 1982. Mobility of herbicides in soil columns under saturated- and unsaturated-flow conditions. Weed Sci. 30(6): 579-584.

Wuu, K.D. and W.F. Grant. 1966. Morphological and somatic chromosomal aberrations induced by pesticides in barley (Hordeum vulgare). Can. J. Genet. Cytol. 8(3): 481-501.

Wuu, K.D. and W.F. Grant. 1967. Chromosomal aberrations induced by pesticides in meiotic cells of barley. Cytologia. 32: 31-41.

Zandvoort, R., G.W. van den Born, J.M. Braber and J.H. Smelt. 1980. Leaching of the herbicide bromacil after application on railroads in the Netherlands. Water Air Soil Pollut. 13(3): 363-372.

Zimdahl, R.L., V.H. Freed, M.L. Montgomery and W.R. Furtick. 1970. Degradation of triazine and uracil herbicides in soil. Weed Res. 10(1): 18-26.

APPENDIX

This profile is based on data identified by computerized literature searches of:

CA SEARCH (Files 308, 309, 310, 311, 320)
TOXLINE
MEDLINE
RTECS
SCI SEARCH
OHM TADS
STORET
SRC Environmental Fate Data Bases
SANSS
AQUIRE
EPCASR
Chemical Industry Notes

Most of these searches were conducted in February, 1983; a few were conducted March-May, 1983. In addition, hand searches were made of Chemical Abstracts (Collective Indices 7 and 8th), and the following secondary sources were reviewed:

ACGIH (American Conference of Governmental Industrial Hygienists). 1980. TLVs: Documentation of the Threshold Limit Values. 4th ed. (Includes Supplemental Documentation, 1981). Cincinnati, OH. 486 p.

ACGIH (American Conference of Governmental Industrial Hygienists). 1982. Documentation of the Threshold Limit Values for Chemical Substances in Work Air. Cincinnati, OH. 94 p.

Bruin, P., G.J. Bergen and J.J. Desta, Ed. 1980. Handling Chemicals Safely. 2nd ed. Dutch Assoc. of Safety Experts, Dutch Chemical Industry Assoc., and Dutch Safety Institute, The Netherlands. 1013 p.

Clayton, G.D. and F.E. Clayton, Ed. 1981. Patty's Industrial Hygiene and Toxicology. 3rd rev. ed. Vol. 2A. John Wiley and Sons, NY. 2878 p.

Clayton, G.D. and F.E. Clayton, Ed. 1981. Patty's Industrial Hygiene and Toxicology. 3rd rev. ed. Vol. 2B. John Wiley and Sons, NY. 2879-3816 p.

Clayton, G.D. and F.E. Clayton, Ed. 1982. Patty's Industrial Hygiene and Toxicology. 3rd rev. ed. Vol. 2C. John Wiley and Sons, NY. 3817-5112 p.

Hamilton, A. and H.L. Hardy. 1974. Industrial Toxicology. 3rd ed. Publishing Sciences Group, Inc., MA. 575 p.

ITII (International Technical Information Institute). 1982. Toxic and Hazardous Industrial Chemicals Safety Manual for Handling and Disposal with Toxicity and Hazard Data. ITII, Tokyo, Japan. 700 p.

Muir, G.D., Ed. 1977. Hazards in the Chemical Laboratory. 2nd ed. The London Chemical Society, London. 473 p.

NTP (National Toxicology Program). 1982. Carcinogenesis Testing Program. Chemicals on Standard Protocol. Management Status. Report date: December 31, 1982.

Proctor, N.H. and J. P. Hughes. 1978. Chemical Hazards of the Workplace. J.B. Lippincott Co., Philadelphia. 533 p.

Sax, I.N. 1979. Dangerous Properties of Industrial Materials. 5th ed. Van Nos Reinhold Co., NY.